

REMARKS

I. Introduction

In response to the Office Action dated March 10, 2004, claim 14 has been amended. Claims 13-15 remain in the application. Reconsideration of the application, as amended, is requested.

II. Claim Amendments

Applicants' attorney has made amendments to the claims as indicated above. These amendments were made solely for the purpose of clarifying the language of the claims, and were not required for patentability or to distinguish the claims over the prior art. Claim 14 was amended merely to clarify that the HIV referred to in claim 13 was the HIV vector. This amendment introduces no new matter, and entry of the amendment is respectfully requested.

III. Claim Rejections

On page (2) of the Office Action, claims 13-15 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. On page (4) of the Office Action, claim 14 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse the first rejection, for the reasons discussed below. Claim 14 has been amended to overcome the latter rejection by clarifying that the HIV referred to in claim 13 was the HIV vector.

As stated at page 4 of the Office Action, the enablement rejection is based on lack of predictability in the art, a limited amount of direction given, the state of the prior art with regard to model systems and correlating *in vitro* effects with *in vivo* effects, the quantity of experimentation needed, and the lack of applicable working examples. At page 3, the Examiner notes that successful implementation of viral vector administration for inhibiting HIV replication *in vivo* in a subject was not routinely achievable by those skilled in the art and, as of the year 2000, lentiviral vectors had not been used in clinical trials. The Examiner cites a reference detailing practical and safety-related reasons why the author believes the HIV-1 lentiviral vector system is unlikely to be used in humans for therapy (although these practical concerns do not relate to the technical merits of being able to

use HIV-based vectors to inhibit HIV replication *in vivo*). The Examiner further notes that *in vitro* effects are not very often predictive of *in vivo* effects and animal model systems for HIV infection are lacking.

The rejection appears to be based on an alleged lack of utility, as indicated by the Examiner's assertion that one of skill in the art could not use the claimed method to treat an HIV infection in a subject. The rejection is not based on an assertion that one skilled in the art would be unable to make the recited HIV vector or to carry out the claimed method for using the HIV vector; rather, the rejection is based on an inference that the skilled artisan would not be able to use the claimed invention because of the lack of evidence that the claimed invention would work in human subjects.

As such, a rejection based on lack of utility, whether grounded upon §101 or §112, first paragraph, rests on the same basis: that the asserted utility is not credible. See MPEP §2164.07 (Section I.A.). According to MPEP §2164.07, a §112, first paragraph, rejection should not be imposed or maintained unless an appropriate basis exists for imposing a rejection under §101 under the guidelines set forth therein. In accordance with these guidelines, evidence relating to utility will be sufficient if, considered as a whole, it would lead a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true.

The Office Action suggests that the *in vitro* data provided in the Examples are insufficient and implies that direct evidence of efficacy in human subjects is required. The requirement for enabling disclosure of a claimed invention, however, does not require definitive proof. "[S]ection 112 does not require that a specification *convince* persons skilled in the art that the assertions therein are correct" (*In re Robins*, 166 USPQ 552, 556, CCPA 1970). The proper question is whether the person skilled in the art, viewing the evidence and state of the art as a whole, would believe that the claimed invention can be used for treatment of HIV infection with a reasonable expectation of success.

Claim 13 is directed to a method for treating a host infected with a human immunodeficiency virus (HIV) comprising exposing said host to an amount of HIV vector effective to inhibit HIV replication, and a biologically acceptable carrier, excipient and diluent. The HIV vector lacks a

transgene and has an intact 5' HIV LTR, a lentiviral packaging signal sequence that comprises the leader sequence downstream of the LTR and until the beginning of the gag gene, and the rev response element, and has 124 base pairs of nef sequences upstream of the 3' LTR replaced with a polylinker. There is no question that the specification teaches how to construct and administer such a vector. The Examiner acknowledges that Example 2 demonstrates that a vector of the invention is capable of inhibiting HIV-1 replication in lymphocytes transduced by HIV-1. Thus, the only issue is whether this demonstration that the HIV vector recited in the claims inhibits HIV replication *in vitro* creates a reasonable expectation that it would also inhibit HIV replication *in vivo*.

By noting that *in vitro* data are often not predictive of *in vivo* effects and that animal model systems for HIV infection are lacking, the Patent Office appears to be requiring clinical data demonstrating efficacy in human subjects. In the absence of such data, the Office apparently takes the position that one skilled in the art would not have a reasonable expectation of success in using a modified HIV vector to inhibit HIV replication.

The claimed invention is not to cure or eradicate HIV. The claimed method treats HIV infected individuals by inhibiting HIV replication. This is not an outrageous or preposterous strategy for treating HIV-infected individuals (see press releases and news articles submitted herewith as Exhibits 1-3). To regard the claimed method as unpatentable because it lacks credibility simply because there is no suitable substitute for clinical trials, places an impossible burden on the Applicants (due to the impracticality of obtaining and waiting for clinical trial results) and defeats the purpose of the patent system to promote progress in the useful arts.

Because the specification provides data establishing that an HIV vector modified as recited in the claims is capable of inhibiting HIV replication in human lymphocytes transduced by HIV-1, the specification provides adequate support to enable the subject matter of claims 13-15. The data presented in Example 2 of the specification show that the claimed method is specific to the treatment, effective with increasing amounts of HIV virus challenge, results in no cytopathic effects in the lentivector transduced cells, and results in more cells being transduced by the lentivector at 13 days survival. Accordingly, these *in vitro* data offer strong support for the claimed method of inhibiting HIV replication.

The Examiner is respectfully requested to reconsider and withdraw the enablement rejection.

IV. Conclusion

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

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